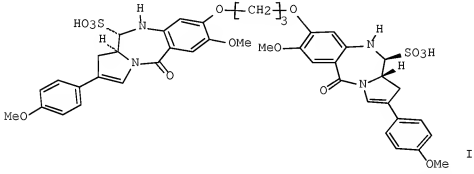
L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2009:1316122 CAPLUS Full-text
DN 152:74989
TI Synthesis of a novel C2/C2'-aryl-substituted pyrrolo[2,1-c][1,4]benzodiazepine dimer prodrug with improved water solubility and reduced DNA reaction rate
AU Howard, Philip W.; Chen, Zhizhi; Gregson, Stephen J.; Masterson, Luke A.; Tiberghien, Arnaud C.; Cooper, Nectaroula; Fang, Min; Coffils, Marissa J.; Klee, Sarah; Hartley, John A.; Thurston, David E.
CS The School of Pharmacy, Spirogen Ltd, London, WC1N 1AX, UK
SO Bioorganic & Medicinal Chemistry Letters (2009), 19(22), 6463-6466
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
GI



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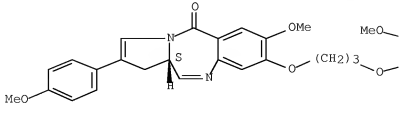
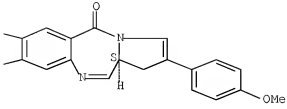
AB A prodrug form I·Na of a novel C2/C2'-aryl-substituted pyrrolobenzodiazepine (PBD) dimer II has been synthesized by introducing sodium bisulfite groups to the C11/C11'-positions of the parent bis-imine. The prodrug form is highly water soluble, stable in aqueous conditions, and the rate of DNA cross-link formation is much slower compared to the parent bis-imine.
IT 864754-68-7P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antitumor activity of aryl-substituted pyrrolobenzodiazepine dimer via cyclization, triflation and Suzuki coupling of nitrobenzoic acid dimer with methoxyphenylboronic acid followed by formation of the bisulfite adduct)
RN 864754-68-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,11a-dihydro-7-methoxy-2-(4-methoxyphenyl)-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A





RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2006:1124678 CAPLUS Full-text
DN 145:455035
TI Preparation of pyrrolobenzodiazepine derivatives for treatment of proliferative diseases
IN Gregson, Stephen John; Howard, Philip Wilson; Chen, Zhizhi
PA Spirogen Limited, UK
SO PCT Int. Appl., 77pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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PI	WO 2006111759	A1	20061026	WO 2006-GB1456	20060421
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	JP 2008536905	T	20080911	JP 2008-507165	20060421
	NZ 563136	A	20091127	NZ 2006-563136	20060421
	AT 452898	T	20100115	AT 2006-726846	20060421
	IN 2007DN07862	A	20071109	IN 2007-DN7862	20071011
	US 20080167293	A1	20080710	US 2007-911890	20071018
	US 7612062	B2	20091103		
	MX 2007013039	A	20080313	MX 2007-13039	20071019
	CN 101171257	A	20080430	CN 2006-80015716	20071108
	ZA 2007009615	A	20081126	ZA 2007-9615	20071108
	KR 2008004618	A	20080109	KR 2007-727047	20071120
PRAI	GB 2005-8084	A	20050421		
	GB 2005-22746	A	20051107		
	WO 2006-GB1456	W	20060421		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS CASREACT 145:455035; MARPAT 145:455035
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. with general formula I [wherein: R2 = (un)substituted aryl; R6 and R9 = independently H, R, OH, OR, SH, SR, NH2, NHR, NRR', nitro, Me3Sn, or halo, where R and R' = independently (un)substituted alkyl, heterocyclyl,

or aryl; R7 = H, R, OH, OR, SH, SR, NH2, NHR, NHRR', nitro, Me3Sn, or halo; Z = alkylene; X = O, S, or NH; n = 2 or 3] or pharmaceutically acceptable salts or solvates thereof are prepared for the treatment of proliferative diseases. For example, compound II•2Na was prepared in a multi-step synthesis. II•2Na showed IC50 of 1.5 nM in the In Vitro cytotoxicity test with K562 human chronic myeloid leukemia cells.

IT 913262-25-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

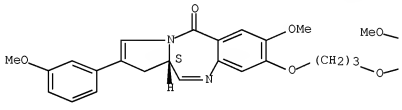
(preparation of pyrrolobenzodiazepine derivs. for treatment of proliferative diseases)

RN 913262-25-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,11a-dihydro-7-methoxy-2-(3-methoxyphenyl)-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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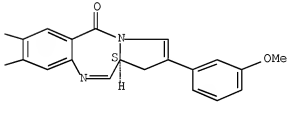


IT 864754-68-7P 913262-40-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

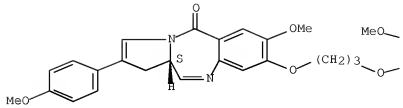
(preparation of pyrrolobenzodiazepine derivs. for treatment of proliferative diseases)

RN 864754-68-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,11a-dihydro-7-methoxy-2-(4-methoxyphenyl)-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



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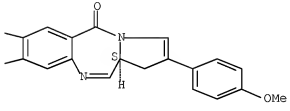
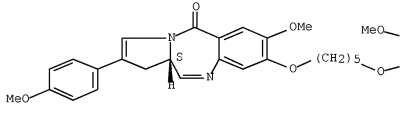


RN 913262-40-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one,
8,8'-[1,5-pentanediylbis(oxy)]bis[1,11a-dihydro-7-methoxy-2-(4-methoxyphenyl)-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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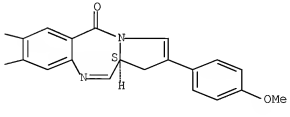

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2010 ACS on STN
AN 2005:1004748 CAPLUS Full-text
DN 143:306348
TI Preparation of pyrrolobenzodiazepinone derivatives as antitumor agents
IN Howard, Philip Wilson; Gregson, Stephen John
PA Spirogen Limited, UK
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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PI	WO 2005085251	A1	20050915	WO 2005-GB768	20050301
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	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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	CA 2558195	A1	20050915	CA 2005-2558195	20050301
	EP 1720881	A1	20061115	EP 2005-717846	20050301
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	JP 2007525535	T	20070906	JP 2007-501340	20050301
	US 20070173497	A1	20070726	US 2007-598518	20070206
PRAI	GB 2004-4575	A	20040301		
	GB 2004-26392	A	20041201		
	WO 2005-GB768	W	20050301		

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT
OS CASREACT 143:306348; MARPAT 143:306348
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = labile leaving group, alkenyl or substituted phenyl; R2 and R5 independently = H, OH, SH, etc.; R3 and R4 independently = H, NH2, halo, etc. or the compound is a dimer with each monomer being of formula I, where the R3 and R4 groups of each monomer form together a dimer bridge -X-R-X-; R = alkylene group, which may be interrupted by heteroatoms or aromatic rings; X = O, S or NH; R6 = carbamate-based N-protecting group; R7 = oxygen protecting group or OH or R6 and R7 together form double bond between N10 and C11] and their pharmaceutically acceptable salts, are prepared and disclosed as antitumor agents. Thus, e.g., II was prepared by palladium catalyzed coupling of III (preparation given) with trans-propenylboronic acid followed by deprotection. The in vitro cytotoxicity of I towards K562 human chronic myeloid leukemia cells was evaluated using ELISA assay and it was revealed that selected compds. of the invention displayed IC50 values of less than 1 μM. I should prove useful in the treatment of proliferative diseases such as leukemia. Pharmaceutical comprns. comprising I are disclosed.
IT 864754-68-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

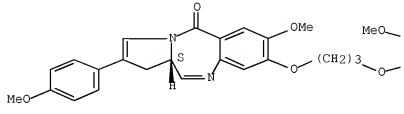
(preparation of pyrrolobenzodiazepinone derivs. as antitumor agents)

RN 864754-68-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,11a-dihydro-7-methoxy-2-(4-methoxyphenyl)-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



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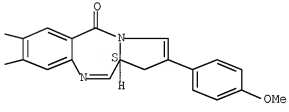

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L2              QUE L1
L3            1 S L2
L4            3 S L2 FUL

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Structure attributes must be viewed using STN Express query preparation.
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L1              STRUCTURE UPLOADED
L2              QUE L1
L3            1 S L2
L4            3 S L2 FUL

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L5            3 S L4

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L1              STRUCTURE UPLOADED
L2              QUE L1
L3            1 S L2
L4            3 S L2 FUL

     FILE 'CAPLUS' ENTERED AT 16:24:28 ON 05 FEB 2010
L5            3 S L4

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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